REMARKS/ARUGMENTS

Upon entry of this amendment, claims 1, 3-7 and 9-14 will be amended and claims 15-20 will be added, whereby claims 1-20 will be pending. Claims 1, 11 and 13 are independent claims.

Applicants note that the claims have been amended to address the 35 U.S.C. 112, second paragraph, rejection. Moreover, claims 15-19 have been added to include additional claims in accordance with the originally presented multiple dependent claims. Still further, claim 20 has been added in accordance with Applicants' originally presented disclosure, and which is directed to an *in vitro* cell capable of inducing cellular immunity, the *in vitro* cell comprising a complex comprising a hydrophobized polysaccharide, an antigen and an antigen-presenting cell. In this regard, while the claim recites an *in vitro* cell, it is noted that this cell can be inserted into a body.

Reconsideration and allowance of the application are respectfully requested.

Consideration Of Disclosure Statements

Applicants express appreciation for the inclusion with the Office Action of a copy of initialed copies of the Forms PTO-1449 submitted with Applicants' Information Disclosure Statement, filed July 9, 2001, and Supplemental Information Disclosure Statement, filed August 8, 2003, whereby the Examiner's consideration of these disclosure statements is of record.

However, upon review of the initialed forms, it is noted that the Examiner has only initialed the English language abstracts for WO98/09650 and WO92/04887 and has not initialed the Japanese documents Byotai Seiri and JP61-69801, JP63-319046, JP3-292301, JP7-97333 and JP7-206903.

With respect to the above, Applicants respectfully submit that each of the documents contains an English abstract, is cited in a communication from a foreign office action which is written in English, and/or the documents are cited and discussed in the specification, at pages 2-3 and page 6. In particular:

WO98/09650 is accompanied by an English abstract, is cited in the International Search Report of which an English copy has been provided, and Statement and is cited and discussed in the specification beginning at page 3. Moreover, the national stage U.S. application of the international application that published as WO 98/09650 was submitted in the Supplemental Information Disclosure Statement;

WO92/04887 is accompanied by an English abstract, is cited in the International Search Report of which an English copy has been provided and the document is cited and discussed in the specification beginning at page 3;

JP 61-69801 is accompanied by an English Abstract and is cited and discussed in the specification beginning at page 3;

JP 63-319046 is accompanied by an English Abstract and is cited and discussed in the specification beginning at page 3;

JP 3-292301 is accompanied by an English Abstract and is cited and discussed in the specification beginning at page 6;

JP 7-97333 is accompanied by an English Abstract and a Patent Abstracts of Japan and is cited and discussed in the specification beginning at page 6;

JP 7-206903 is accompanied by an explanation thereof and a Patent Abstracts of Japan; and

Byotai Seiri (Pathophysiology), Vol. 6, No. 10, pp. 771-780 (1987), is accompanied by an English translation of Fig. 5 at page 776 thereof.

Still further, the initialed forms confirm the Examiner's consideration of the English abstracts, and it is respectfully requested that the crossed through documents be initialed in order that these documents will appear on the face of the issued patent along with the English abstracts. Applicants are therefore submitting an additional Form PTO-1449 citing the crossed through documents. The Examiner is therefore respectfully requested to forward an initialed copy of the form with the next communication from the Patent and Trademark Office.

If the Examiner deems that any further information is necessary, the Examiner is respectfully requested to contact the undersigned by telephone to discuss the same.

Response to Formal Matters

Applicants express appreciation for the acknowledgment in the Office Action of the claim of foreign priority as well as receipt of the certified copy of the priority document in this national stage application.

Applicants note that the Office Action does not object to the drawings submitted with the application. Therefore, in the absence of any further indication of any informality in the drawings, Applicants assume that the drawings are in compliance with all formality requirements.

Response To Rejection Under 35 U.S.C. 112, Second Paragraph

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The rejection asserts that claims 1-10, while appearing to be intended to recite an antigen presenting cell, would also encompass T cells. Further, with respect to claims 11-12, the rejection asserts that, even though the claimed method would require the action of a T cell, no such T cell is included in any step of the claimed method. With respect to claims 3-14, the rejection asserts that these claims are vague in use of the term "characterized in."

In response, Applicants respectfully submit that one having ordinary skill in the art would readily understand the meaning of the terminology utilized in the claims, and that the claims clearly and definitely recite Applicants' invention. However, in an attempt to advance prosecution the claims have been amended herein to include what should be considered to be cosmetic changes therein to even present Applicants' invention in a clearer manner.

For examples, claim 1 has been clarified to even more clearly indicate that it is directed to a cell capable of inducing cellular immunity, the cell being produced by reacting *in vitro* a complex comprising a hydrophobized polysaccharide and an antigen with an antigen-presenting cell.

Claim 11 has been clarified to even more clearly indicate that it is directed to a method for preparing a cell capable of inducing cellular immunity comprising reacting *in vitro* a complex comprising a hydrophobized polysaccharide and an antigen with an antigen-presenting cell.

Regarding the terminology "characterized in", Applicants have amended to claims to avoid use of such terminology even though such terminology is clear and definite.

In view of the above, the indefiniteness rejection should be withdrawn.

Response To Rejections Based Upon Prior Art

Prior to addressing the rejections of record, Applicants note that the Office Action states that the cell of claims 1-10 is considered to be an activated T cell. Further, the Office Action states that while the claims recite a product-by-process, there is no evidence that the process results in a novel activated T cell. Accordingly, the Office Action states that the claims are considered to encompass any activated T cell.

In response to the above and prior to discussing the specifically set forth rejections, Applicants note that claims 1-10 are not directed to a T cell, but are directed to a cell capable of inducing cellular immunity, said cell being produced by reacting *in vitro* a complex comprising a hydrophobized polysaccharide and an antigen with an antigen-presenting cell. In other words, the cell of the present invention is formed *in vitro*, and can is administered to induce cellular immunity *in vivo*.

Rejection Of Claims 1-10 Under 35 U.S.C. § 102(e) as being clearly anticipated by U.S. Patent No. 6,319,709 to Ostrand-Rosenberg.

In response to the rejection of claims 1-10 under 35 U.S.C. § 102(e) as being clearly anticipated by U.S. Patent No. 6,319,709 to Ostrand-Rosenberg, Applicants respectfully submit the following.

Initially, Applicants note that Ostrand-Rosenberg is applied as 35 U.S.C. 102(e) prior art. However, Applicants note that this document indicates that it is a continuation of Application No. 09/159,135, filed September 23, 1998, which matured into U.S. Patent No. 6,149,905, which is a

division of Application No. 08/147,772, filed November 3, 1993, which matured into U.S. Patent No. 5,858,776. In order that the record is complete, Applicants are submitting copies of these other patents.

Moreover, it appears that this rejection is based upon the above-noted assertion in the Office Action that the claims are considered to encompass any activated T cell.

Applicants note that the rejection points to the disclosure of Ostrand-Rosenberg at column 16, lines 34-64. It is noted that this disclosure is directed to another approach of Ostrand-Rosenberg for inducing or enhancing an anti-tumor T cell-mediated immune response by triggering a costimulatory signal in T cells is to obtain T lymphocytes from a tumor-bearing subject and activate the cells *in vitro* by contact with a tumor cell and a stimulatory form of a costimulatory molecule. In this embodiment, it is disclosed that T cells can be obtained from a subject, and the sample fractionated to remove red blood cells and enrich or isolate T lymphocytes or T lymphocyte subpopulations. It is disclosed that T cells can be activated *in vitro* by culturing the T cells with tumor cells obtained from the subject together with a stimulatory form of a costimulatory molecule or, alternatively, by exposure to a modified tumor cell as described in Ostrand-Rosenberg. The term "stimulatory form" is defined by the costimulatory molecule being capable of crosslinking its receptor on a T cell and triggering a costimulatory signal in T cells. The stimulatory form of the costimulatory molecule is disclosed to be, for example, a soluble multivalent molecule or an immobilized form of the costimulatory molecule, for instance coupled to a solid support. It is also disclosed that fragments, mutants or variants of costimulatory molecules which retain the ability to trigger a costimulatory signal in T cells can also be used. It is also disclosed that in a preferred

embodiment, a soluble extracellular portion of B7 is used to provide costimulation to the T cells. Following culturing of the T cells *in vitro* with tumor cells and a costimulatory molecule, or a modified tumor cell, to activate tumor-specific T cells, it is disclosed that the T cells can be administered to the subject, for example by intravenous injection.

Thus, from a review of this disclosure, it is seen that Ostrand-Rosenberg may disclose *in vitro* action of tumor specific T lymphocytes. However, the rejection does not point out where Ostrand-Rosenberg teaches each of the features recited in Applicants' claims. Ostrand-Rosenberg dos not appear to teach each and every feature recited in Applicants' independent claim 1 and as further defined in the dependent claims. In particular, Ostrand-Rosenberg does not disclose a a cell capable of inducing cellular immunity, the cell being produced by reacting *in vitro* a complex comprising a hydrophobized polysaccharide and an antigen with an antigen-presenting cell.

If this ground of rejection is maintained, Applicants respectfully request that the rejection specifically indicate where each of Applicants' recited features is disclosed in Ostrand-Rosenberg.

Applicants respectfully request withdrawal of this ground of rejection.

Rejection Of Claims 1-10 Under 35 U.S.C. § 102(b) as being clearly anticipated by Gu et al., Cancer Research 58,3385-3390, August 1988

In response to the rejection of claims 1-10 under 35 U.S.C. § 102(b) as being clearly anticipated by Gu et al. (hereinafter "Gu"), Applicants respectfully submit the following.

Initially, as with the rejection based upon Ostrand-Rosenberg, Applicants note that this rejection appears to be based upon the above-noted assertion in the Office Action that the claims are considered to encompass any activated T cell.

In this ground of rejection, it is asserted that Gu teaches a T cell activated with a tumor antigen, with Gu page 3386, column 2, last paragraph, being specifically referenced.

Gu discloses a hydrophobized polysaccharide-antigen complex which is injected into an animal. Gu teaches the extraction of CTL's from the marrow of the inoculated animal. Gu does not disclose each and every feature recited in Applicants' independent claim 1 and as further defined in the dependent claims. In particular, Gu does not disclose, amongst other features, a cell capable of inducing cellular immunity, the cell being produced by reacting *in vitro* a complex comprising a hydrophobized polysaccharide and an antigen with an antigen-presenting cell.

To further denote differences between the presently claimed invention and Gu, Applicants are submitting further information regarding the subject matter as disclosed in Gu. In particular, Applicants are submitting herewith copies of Wang et al., International Journal of Oncology 14, 695-701, 1999 and Ikuta et al., Blood, 15 May 2002, Volume 99, No. 10.[1] Applicants' invention comprises the inclusion of an antigen-presenting cell with a complex comprising a hydrophobized polysaccharide and an antigen. As can be seen in Fig. 1 of Wang et al. (which is similar to Fig. 5 of Gu for CHM-HER2 instead of CHP-HER2 in Wang et al.) as compared to Fig. 5 of Wang et al.,

---

1 These documents are submitted as evidence directed to an issue of patentability raised in an Office Action. Accordingly, payment of a fee should not be necessary for consideration of these documents. See M.P.E.P. §609C(3). Of course, if any fee is believed to be necessary for consideration of these documents, the Commissioner is hereby authorized to charge appropriate fees to Deposit Account No. 19-0089.

dentritic cell pretreated CHP-CAB complexes provide tumor suppression even after 10 days whereas unpretreated CHP-CAB complexes show tumor suppression through 3 days. This is further evidence of the structural and advantageous differences between Applicants' invention and that disclosed by Gu.

In view of the above, Applicants respectfully request withdrawal of this ground of rejection.

Rejection Of Claims 13-14 Under 35 U.S.C. § 103(a) as being unpatentable over Nestle et al., Nature Medicine, Vol. 4, No. 3, pp. 328-332 (1998) in view of Jiang et al., Nature, Vol. 375, 11 May 1995, pp. 151-155

In response to the rejection of claims 13 and 14 under 35 U.S.C. § 103(a) as being unpatentable over Nestle et al. (hereinafter "Nestle") in view of Jiang et al. (hereafter "Jiang"), Applicants respectfully submit the following.

This ground of rejection asserts that Nestle teaches a method for inducing cellular immunity comprising isolating an APC, reacting said APC with a tumor antigen, and returning the cell to the living body by parenteral administration. The rejection asserts that Nestle differs from the claimed invention only in that it does not teach the reaction of the APC with a complex comprising a hydrophobized polysaccharide. However, the rejection asserts that Jiang teaches that the dendritic cell homolog of the macrophage mannose receptor can facilitate a 100-fold increase in the uptake and presentation of antigen by a dendritic cell. The rejection concludes that it would have been obvious to one of ordinary skill in the art to perform a method for inducing cellular

immunity comprising isolating an APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle, including a hydrophobized polysaccharide complex in the reacting of the antigen with the APC. The rejection asserts that one of ordinary skill in the art at the time of the invention would have been motivated to add a mannan complex to the reaction because said addition would have been expected to increase the uptake and presentation by the dentritic cell, given the teachings of Jiang that activation of the dentritic cell homolog of the macrophage mannose receptor can facilitate a 100-fold increase in the uptake and presentation of antigen by a dentritic cell.

In contrast to the assertions in the rejection, Applicants note that Applicants' independent claim 13 is directed to a method for inducing cellular immunity *in vivo* comprising isolating an antigen-presenting cell from a living body, reacting a complex comprising a hydrophobized polysaccharide and an antigen with the antigen-presenting cell, and returning the resulting cell to the living body. Dependent claim 14 further defines that the returning the antigen-presenting cell to the living body comprises returning the antigen-presenting cell by parenteral administration.

As can be seen from Applicants' claims, amongst other features recited therein Applicants claims include a method for inducing cellular immunity *in vivo* comprising isolating an antigen-presenting cell from a living body and reacting a complex comprising a hydrophobized polysaccharide and an antigen with the antigen-presenting cell.

Applicants respectfully submit that one having ordinary skill in the art would not have been motivated to combine the disclosures of Nestle and Jiang. However, even if for the sake of argument, the disclosures were combined, Applicants note that neither of Nestle nor Jiang

discloses reacting a complex comprising a hydrophobized polysaccharide and an antigen with the antigen-presenting cell. Therefore, no combination of Nestle and Jiang would include a hydrophobized polysaccharide-antigen complex. For example, Jiang teaches that antigen presenting functions of dendritic cells is associated with the high-level expression of a specific receptor, DEC-205. Nestle teaches that the *in vitro* creation of an antigen-dendritic cell yields an increase in the immune response of inoculated patients. The combination of these two documents would at most lead to an antigen-dendritic cell overexpressing DEC-205, and not the currently claimed method including a hydrophobized polysaccharide-antigen-cell complex.

For the reasons set forth above, Applicants' claimed invention is not taught or suggested by the prior art, whereby the claims are patentable over the prior art of record, and the rejections should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
Hiroshi SHIKU et al.

Bruce H. Bernstein
Reg. No. 29,027

M-1111

January 13, 2004
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191